THE AGING BRAIN | BLOOD-SUGAR LEVELS | TUMOUR SUPPRESSORS

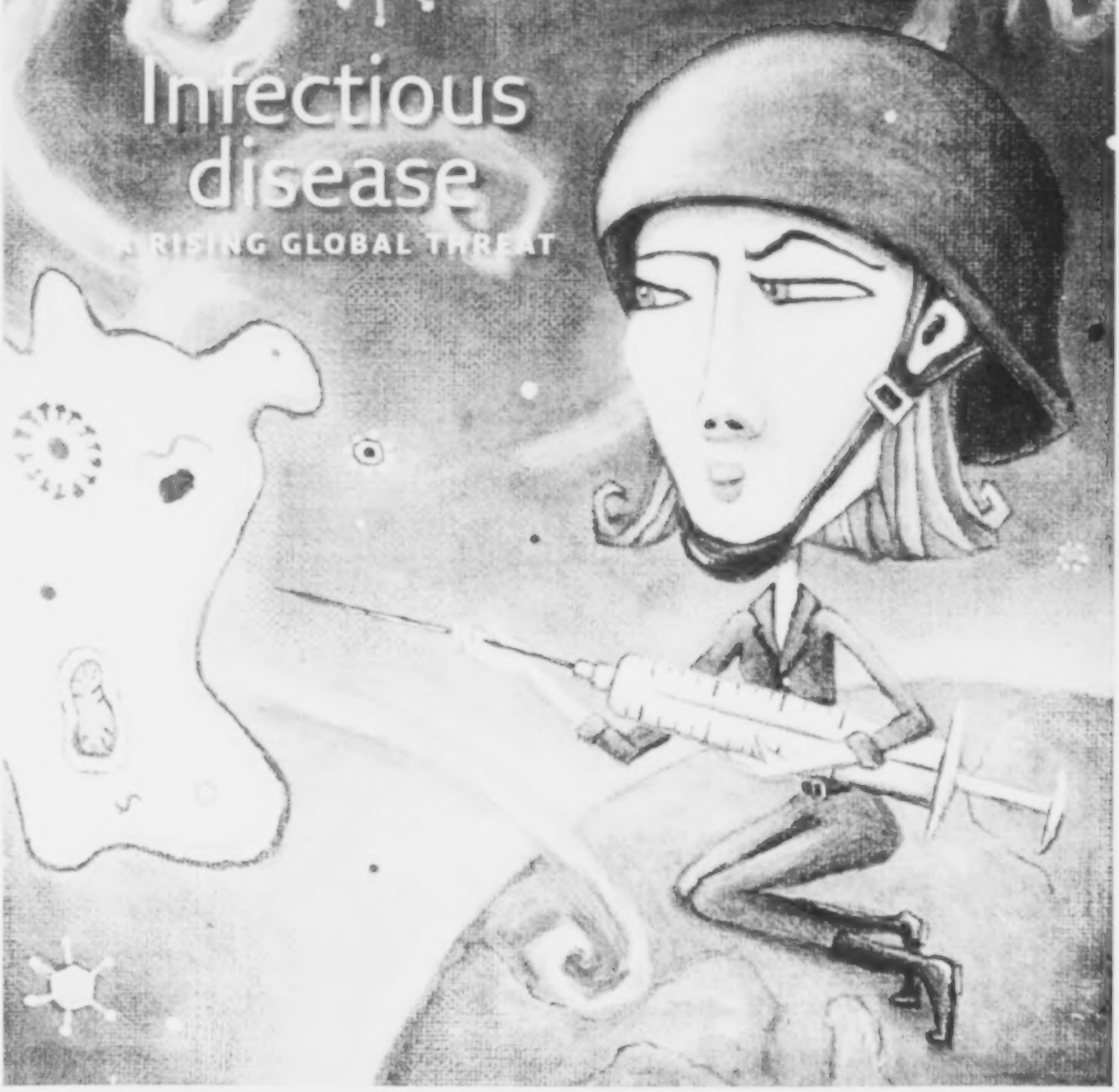
ResearchNews

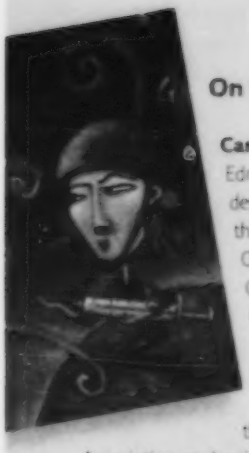
ALBERTA HERITAGE FOUNDATION FOR MEDICAL RESEARCH

WINTER 2008

Infectious disease

A RISING GLOBAL THREAT





On the cover

Carla Andrew is an Edmonton-based artist, designer, and illustrator and the owner of Brio Studios. Originally from Trinidad, Carla studied Visual Communication Design at Grant MacEwan College. Her clients have included Edmonton Tourism, the Downtown Business Association, and various publications and festivals in Edmonton. Carla's website is **www.briostudios.ca**

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ALBERTA HERITAGE FOUNDATION FOR MEDICAL RESEARCH

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We want to hear from you!

Please help us in our efforts to continually improve by telling us what you like and what you don't like about the redesigned *Research News*.

What's in it for you?
Complete our readership survey by April 1, 2008 and your name will be entered to win ***a prize valued at $250***. To access the survey go to **http://www.ahfmr.ab.ca/readershipsurvey/** or call, write, or e-mail us at the address opposite and we would be happy to send you a print version of the survey.

It is only with your help that we can get the information we need to improve the quality of this magazine for all of our readers.

Thank you!

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Making a difference

Dr. Dennis Slamon's breast-cancer research has improved the lives of hundreds of thousands of women

IT'S NOT VERY OFTEN that we get the opportunity to meet a recognized world leader in medical research—someone whose life's work could directly impact our own lives or the lives of people we love.

EACH OCTOBER, however, a Canadian institution called the Gairdner Foundation presents awards to researchers from around the globe for their "major contributions through research to the conquest of disease and the relief of human suffering." The winners participate in a national speaking tour, connecting with the public to talk about their medical breakthroughs. Of the 290 award winners since 1959, the inaugural year, 70 have gone on to receive Nobel Prizes. A prestigious group indeed.

This past fall, Albertans were introduced to Dr. Dennis Slamon of the University of California, Los Angeles, one of the 2007 winners of the Gairdner International Award. Dr. Slamon is a pioneer in the field of targeted therapy for cancer treatment.

In 1986, his group discovered that the tumours of women who suffer from a particularly aggressive form of breast cancer contained too many copies of a gene called HER2, and therefore too many copies of the HER2 protein. Women who have breast cancer and who are also HER2-positive have a median life expectancy less than half that of patients who are HER2-negative. The team still had to show that a causal link existed between the high number of gene copies and the incidence of the cancer. Years of basic-science research made that link clear.

Dr. Slamon is a pioneer in the field of targeted therapy for cancer treatment

Dr. Slamon's research led to the development of the breast-cancer drug Herceptin. The drug binds to the HER2 protein specifically, thus suppressing the growth of cancerous cells. In each phase of drug testing, the cancer was kept at bay. In a very understated fashion, Dr. Slamon explains the impact of this drug: "[Worldwide] there are a million new breast cancers each year. The HER2 alteration is associated with about 200,000 to 250,000. Herceptin will increase the survival of

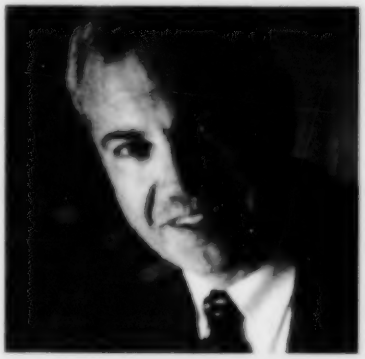
about 30% of those patients." This is a dramatic increase over the 2% to 6% improvement in survival observed using traditional treatments. The bottom line: Dr. Slamon's work has improved the lives of hundreds of thousands of women.

Herceptin represents a new class of cancer therapy. For almost 40 years, oncologists have relied on chemotherapy to treat cancer—either on its own or in combination with surgery or radiation therapy to remove tumours. Dr. Slamon points out that chemotherapies are essentially poisons. Physicians have the delicate task of trying to find the right mix of these poisons in order to kill more bad cells than good cells and minimize serious side effects. "But we're using a non-specific bomb," he says. "It's a pretty primitive therapy when you think about it."

> "Targeted therapy is what the future holds for all medicine"

To break out of the one-size-fits-all therapeutic approach, Dr. Slamon asserts that a shift in thinking was necessary. "Cancer isn't a single disease. Cancer, even within a given organ, is not a single disease. It's diverse. If you accept these principles, then you need therapies that are tailored to the subtype of cancer you're treating.

"Targeted therapy is what the future holds for all medicine," says Dr. Slamon, summarizing the significance of the discovery. Breast cancer has led the field. And we think that with further refinement we can do better than the current survival rates. But that's in progress right now. That's where the excitement is." *



About the researcher
Dr. Dennis Slamon is the chief of hematology-oncology at the University of California, Los Angeles School of Medicine. He received a Gairdner International Award in 2007.

Selected publication
Finn RS, Dering J, Ginther C, Wilson CA, Glaspy P, Tchekmedyian N, Slamon DJ. Dasatinib, an orally active small molecule inhibitor of both the *src* and *abl* kinases, selectively inhibits growth of basal-type/"triple-negative" breast cancer cell lines growing in vitro. *Breast Cancer Research and Treatment.* 2007 Nov;105(3):319-326.

Chromium, stevia, and cinnamon

Nutrition researchers respond to a reader's question about impact on blood-sugar levels

About this feature

AHFMR frequently receives letters requesting information about Heritage research or about various medical conditions. "Responding to the reader" is an *AHFMR Research News* feature intended to provide up-to-date information related to readers' questions, with the help of experts in the Alberta research community. AHFMR cannot provide medical advice, however; please consult your family physician about your specific health concerns.

GLUCOSE IS AN ESSENTIAL FUEL FOR LIFE. Yet almost two million Canadians suffer from type 2 diabetes, a chronic disease in which the cells of the body cannot use glucose for energy. The hormone *insulin* helps transport glucose from the blood into cells. But some people with type 2 diabetes don't make enough insulin; others make it, but their cells don't respond to it, essentially locking glucose out. Consequently, that glucose circulates and builds up in the blood, causing heightened sugar levels and leading to complications such as heart disease, kidney damage, and even blindness.

A READER has asked if research exists on the impact of chromium, stevia, and cinnamon on blood-sugar levels. To find out more, we talked to Dr. Rhonda Bell, an associate professor of human nutrition, and Dr. Catherine Field, a professor of nutrition and metabolism, both based at the University of Alberta.

"Chromium is important for insulin secretion," explains Dr. Bell. "Studies looking at chromium-deficient mice show they have reduced carbohydrate metabolism, which leads to higher blood-glucose levels." And is chromium deficiency a problem in humans? "As a general rule our population has adequate chromium intake," says Dr. Bell. "There may be a genetic subpopulation of type 2 diabetics that can't utilize chromium, and in that case chromium supplementation could be beneficial. We're still too early in the research picture to understand if this subpopulation really exists. I would steer the average person away from supplementing with additional chromium until we know more. It could interfere with the absorption of other important nutrients such as calcium or iron, and cause problems rather than help."

While the picture on chromium is still forming, research on the sweetener stevia is scant at best. There has not yet been a project examining the effect of stevia on blood sugar in humans, but research in rodents shows that it has a negligible effect on blood glucose, even when given in high doses. "Stevia doesn't lower blood sugar levels and it doesn't raise them either," Dr. Field explains. Given that stevia is 300 times sweeter than sugar, it shows promise as a possible substitute for sugar or aspartame. But Dr. Field is quick to caution. "Although stevia is available, it has not been approved for use as a sweetener in Canada. It's probably safe, but it's best to take the 'wait and see' approach."

> "Chromium is important for insulin secretion"

Of the three compounds mentioned in the reader's question, only *Cinnamomum cassia* (the cinnamon found at the grocery store) has been demonstrated to have insulin-like activity. But while some studies show that cinnamon can lower blood sugar, others show that it has no effect. As with chromium, it could be that cinnamon is effective only in certain populations that have yet to be identified. Dr. Field stresses that the amount of cinnamon administered in these studies is high. "People are taking up to twelve 500-milligram capsules per day. We're not looking at a small amount of cinnamon sprinkled on your oatmeal in the morning; these are therapeutic doses."

Both Dr. Bell and Dr. Field agree that no supplement can replace a healthy diet and physical activity, especially when managing type 2 diabetes. ✳

About the researchers
Dr. Catherine Field (L) is a full professor and **Dr. Rhonda Bell** is an associate professor in the Department of Agricultural, Food and Nutritional Science in the Faculty of Agricultural, Life and Environmental Sciences at the University of Alberta. Both Dr. Field and Dr. Bell are also principal investigators with the Alberta Diabetes Institute. They are also part of a team that was recently awarded an ***AHFMR Interdisciplinary Team Grant*** for a project entitled "The impact of maternal nutrient status during pregnancy on maternal and child mental health."

Selected publication
Gougeon R, Spidel M, Lee K, Field CJ. Canadian Diabetes Association National Nutrition Committee technical review: non-nutritive intense sweeteners in diabetes management. *Canadian Journal of Diabetes*. 2004 Dec;28(4):385–399.

Recommended website
The Canadian Diabetes Association
http://www.diabetes.ca

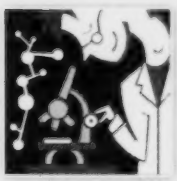
Re-educating the immune system

Dr. Tara Lysechko helps develop hepatitis vaccines as part of a unique program encouraging academic scientists to work in industry

About ForeFront

AHFMR's ForeFront programs work to apply health research into innovative products and services that lead to improved health. For more information go to **http://www.ahfmr.ab.ca/forefront**

AFTER FINISHING HER UNDERGRADUATE SCIENCE DEGREE, Tara Lysechko was eager to work in industry. She was soon hired by a biotechnology company in British Columbia, and her career was launched. Or so she thought.



"I ENJOYED THE WORK, but I could see that an undergraduate degree wasn't going to be enough to ensure a successful career. To get ahead in industry, I needed to further my education." So it was back to the books for a doctorate in immunology from the University of Alberta.

While many people with Ph.D. degrees choose to stay in the academic world, Dr. Lysechko wanted to get her industrial career back on track. As it turned out, she was in the right place at the right time. AHFMR was starting a pilot project to encourage academic scientists to work in Alberta's health industries. Edmonton-based ViRexx Medical Corp., a company that develops therapies for cancer and viral infections, was looking for a scientist to take charge of a key project supporting the development of new therapeutic vaccines for use against the hepatitis B and hepatitis C viruses.

> Dr. Lysechko wanted to get her industrial career back on track

Dr. Lysechko is now working at ViRexx as the first recipient of AHFMR's ForeFront Industrial Research Award.

"The ForeFront award is a win-win for the company and the trainee," says Dr. Lysechko. "ViRexx gets skilled help in the lab. I get valuable industrial research experience."

Dr. Rajan George, ViRexx's senior vice-president and the principal investigator for Dr. Lysechko's project, is just as enthusiastic. "Tara is the perfect fit. She is an immunologist and has experience with the experiments we need to do. Plus, she's committed to working in industry—this is the environment she wants to be in. We're lucky to have her."

Dr. Lysechko's project is part of a comprehensive research program aimed at developing vaccines for the treatment of chronic hepatitis B and C infections. Carriers of these hepatitis viruses have ineffective immune responses that are unable to clear the viruses from their body, leaving them at risk of developing cirrhosis and liver cancer. Worldwide, about one million deaths each year are attributed to liver diseases resulting from chronic hepatitis B infection alone.

"There's been a breakdown in the immune system of chronic hepatitis B carriers," explains Dr. George. "A compromise has been made which allows the virus to persist. Our vaccine is designed to break that compromise and re-educate the immune system so that it recognizes the virus as an outsider, not an insider."

Dr. Tara Lysechko

ViRexx's Chimigen vaccines are designed to take advantage of the two main ways the immune system reacts to *antigens*—foreign substances that, when introduced into the body, stimulate production of antibodies. Chimigen vaccines induce both types of immune response to attack the infectious agent, break tolerance, and eliminate infected cells. The vaccine is made up of two components: one from the virus and the other from an antibody.

> "The ForeFront award is a win-win for the company and the trainee"

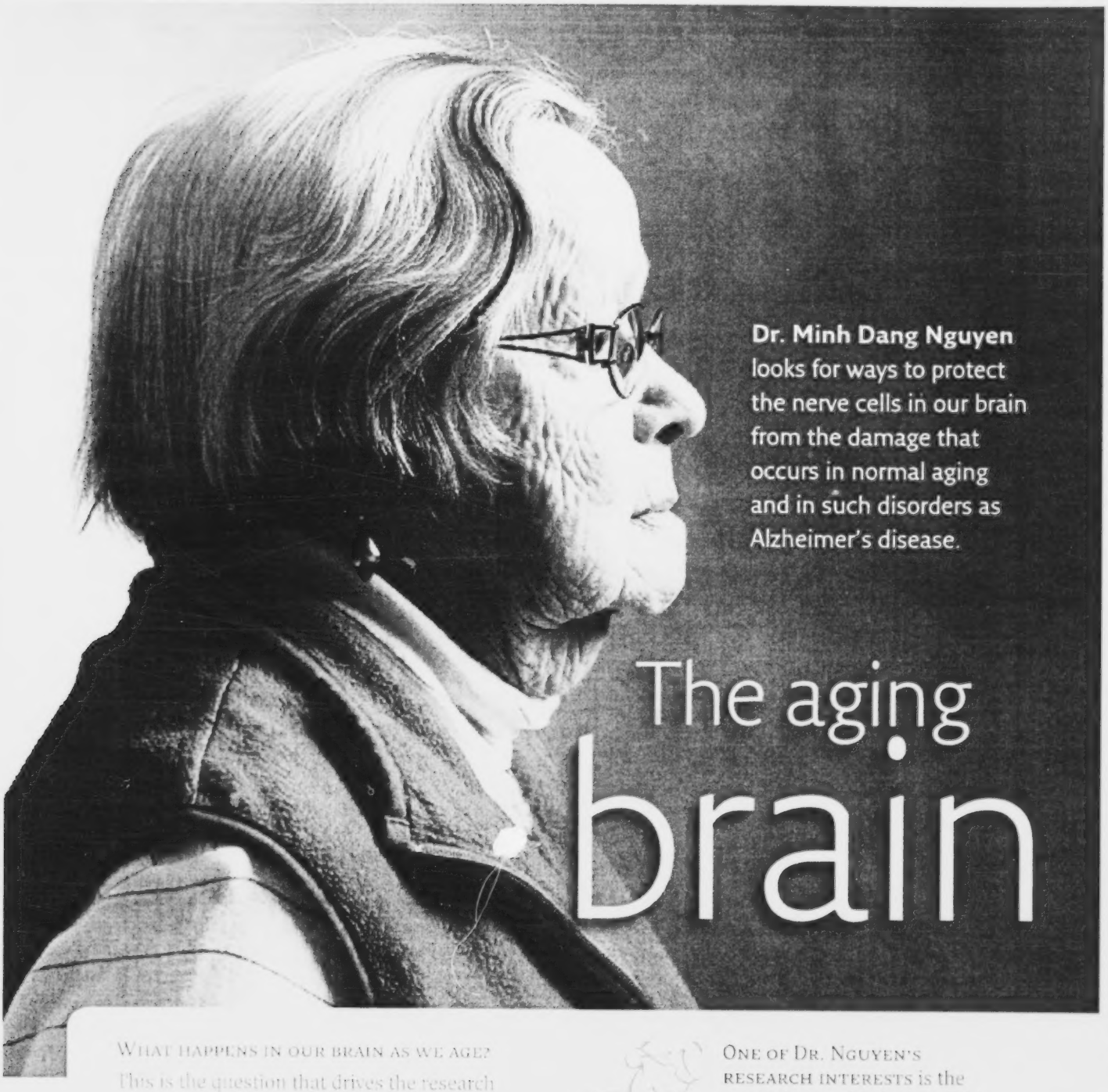
The two are fused into a new protein that the body recognizes as foreign.

"There's no point in giving more antigen to a chronic hep B or hep C carrier—it won't be recognized as foreign," says Dr. George. "With a Chimigen vaccine, chronic carriers receive a new molecule that is recognized as foreign, and this stimulates immune responses against hepatitis B or C."

Dr. Lysechko's experiments are designed to look for these responses in the immune-system cells of chronic hepatitis B or C carriers. She works with immunologist Dr. Bruce Motyka, ViRexx's R&D director, and Dr. Klaus Gutfreund, a consultant hepatologist and an associate professor in the Department of Medicine at the University of Alberta. Dr. Lysechko obtains blood samples from carriers of chronic hepatitis B and C and isolates key cells from the blood. She exposes these cells to the vaccine, and then monitors and measures the immune response. The entire process takes about two weeks per sample.

Results to date are promising. "We are seeing a proliferation of T cells, which means they have recognized the viral antigens as foreign," says Dr. Lysechko. "What we're not sure about is what regions of the antigen the T cells are actually seeing. We'll definitely be following this up.

"Of course, there's still a lot of work to be done, and my project is just one piece of the puzzle. Nonetheless it's exciting to be a part of something that has so much potential. This is where I want to be—working in a team that is translating research into clinical developments that will help people." ✳

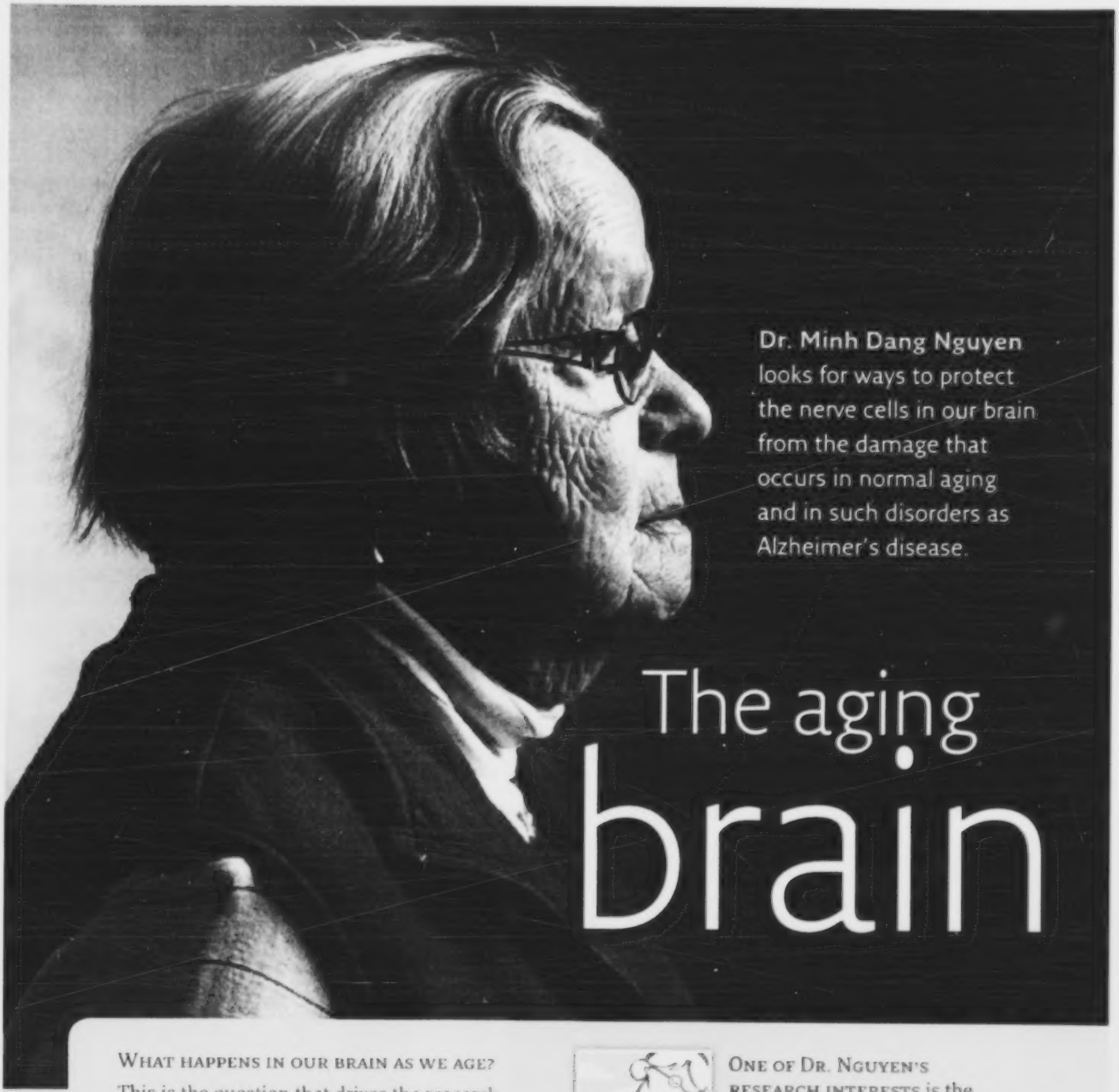


Dr. Minh Dang Nguyen looks for ways to protect the nerve cells in our brain from the damage that occurs in normal aging and in such disorders as Alzheimer's disease.

The aging brain

WHAT HAPPENS IN OUR BRAIN AS WE AGE? This is the question that drives the research of AHFMR Scholar Dr. Minh Dang Nguyen, who arrived at the University of Calgary in September 2005. The main goal in his laboratory is to understand the mechanisms involved in the aging of the brain and in such neurodegenerative disorders as Alzheimer's disease.

ONE OF DR. NGUYEN'S RESEARCH INTERESTS is the *cytoskeleton*, a kind of scaffolding within the nerve cells in the brain (neurons), composed of thread-like structures made of protein. Like any other scaffolding, it provides structure, but it does more than that as well—it transports materials and transmits signals from one part of the cell to another. Changes in the cytoskeleton can lead to such neurodegenerative disorders as Parkinson's disease, amyotrophic lateral sclerosis (also known as ALS, or



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Lou Gehrig's disease), and Charcot-Marie-Tooth disease—an inherited nerve disorder in which patients slowly lose the use of their limbs as the nerves to the extremities deteriorate.

Dr. Nguyen has recently shifted some of his attention to a gene (called *SIRT1*) that has been linked to the aging process and disorders related to it. In a lower organism, such as the fruit fly, increasing the number of copies of this gene extends the fly's lifespan, whereas removing the gene shortens it. This gene is somehow linked also to nutrition: researchers have shown that a low-calorie diet extends the lifespan of fruit flies, except that of flies that have reduced numbers of the gene. Research done on primates shows that the presence of this gene may reduce the incidence of age-related disorders such as certain cancers, type 2 diabetes, and neurodegeneration.

This gene, Dr. Nguyen explains, has stress-sensing properties: when it senses conditions that could cause damage to nerve cells, its levels increase to protect the cells. Aging, however, weakens the cell's defensive response to the point where levels of the gene are too low to fight the toxicity. The balance then shifts, and nerves begin to degenerate.

Dr. Nguyen's research team has recently shown that this gene also protects against the neurodegeneration that occurs in models of Alzheimer's disease and ALS. They treated damaged nerve cells with resveratrol—a substance found in the skins of red grapes (and therefore also in red wine) that activates the gene. "We discovered that if you add this compound to neurons that are starting to degenerate, you can actually rescue them," explains Dr. Nguyen. "The neurons not only survive—behaviour tests of treated animals show that [these neurons] are still functional." This discovery could lead to new treatments for both Alzheimer's and ALS.

Because aging is a topic which touches on many other areas of study, Dr. Nguyen has found no shortage of researchers with whom to collaborate. "The environment at the University of Calgary is very collaborative," says Dr. Nguyen. "That is one of the main reasons I came here." *

Glossary

Neurodegeneration - the progressive damage of nerve cells resulting in gradual decline of the functions controlled by the damaged part of the nervous system

Neuroprotection - the safeguarding of nerve cells from damage

Neurotoxicity - damage to nerve cells

About the researcher
Dr. Minh Dang Nguyen is an *AHFMR Scholar* affiliated with the Hotchkiss Brain Institute at the University of Calgary. He is an assistant professor in the Department of Clinical Neurosciences, Cell Biology and Anatomy, and Biochemistry and Molecular Biology. He also holds the Brenda Stafford Chair in Alzheimer Research.

Selected publications

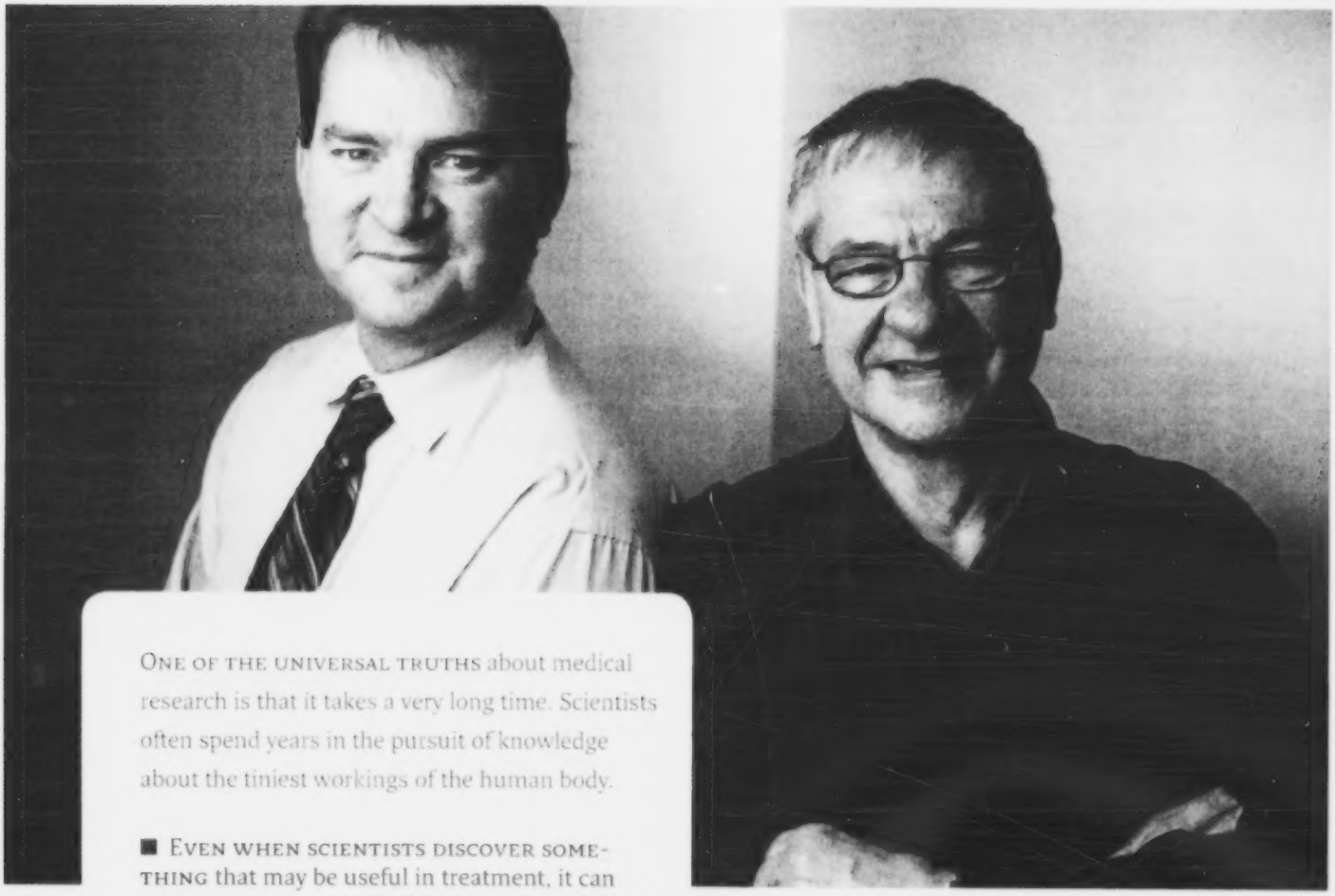
Kim D*, Nguyen MD*, Dobbin MM, Fischer A, Sananbenesi F, Rodgers JT, Delalle I, Baur JA, Sui G, Armour SM, Puigserver P, Sinclair DA, Tsai L-H. SIRT1 deacetylase protects against neurodegeneration in models for Alzheimer's disease and amyotrophic lateral sclerosis. *EMBO Journal*. 2007 July 11; 26(13):3169-3179. *Equal contribution

Nguyen MD, Shu T, Sanada K, Larivière RC, Tseng HC, Park SK, Julien J-P, Tsai L-H. A NUDEL-dependent mechanism of neurofilament assembly regulates the integrity of CNS neurons. *Nature Cell Biology*. 2004 July; 6(7): 595-608.

Recommended website
Dr. Minh Dang Nguyen's laboratory website
http://www.ucalgary.ca/~mdnguyen

Keeping it in the family

A father and son team up to help solve a medical puzzle.



Drs. Peter (L) and David Brindley

ONE OF THE UNIVERSAL TRUTHS about medical research is that it takes a very long time. Scientists often spend years in the pursuit of knowledge about the tiniest workings of the human body.

■ EVEN WHEN SCIENTISTS DISCOVER SOMETHING that may be useful in treatment, it can take many more years before the results of that research are ready for use in your doctor's clinic or in the hospital. This application of scientific findings to treatment—called *translational research*—represents the ultimate goal of medical research: to improve health care and make a difference in people's lives. But the demands of science mean that the journey from bench to bedside, from laboratory to clinic, is long.

Yet there are exceptions to this rule. Just ask AHFMR Scientist and biochemist Dr. David Brindley and his son, critical-care physician Dr. Peter Brindley. For them, it all started in the emergency ward of the University of Alberta Hospital with a critically ill patient thought to be experiencing a complete lack of blood supply to the abdomen—a fatal condition unless surgery could be performed immediately.

However, some strange lab findings gave Dr. Peter Brindley pause: inconsistent lactic acid results. High lactate levels indicated a lack of oxygen in the cells, a finding which would have been expected in a patient lacking blood supply to a particular area. But a different lactate test showed

> The Drs. Brindley dubbed the phenomenon "the lactate gap"

normal levels. Other tests later determined that the patient had swallowed ethylene glycol—a toxic ingredient found in antifreeze and various household cleaners, substances often accidentally swallowed by children. Abdominal surgery could have proven fatal. Instead, the patient was treated for ethylene-glycol poisoning and eventually released.

But the strange lactate-test results continued to puzzle Dr. Peter Brindley. "I've been taught that if things don't fit, you are obligated to find out why. That's science." So he got in touch with a research scientist he happened to know quite well—his father.

Intrigued, Dr. David Brindley suggested conducting some experiments to try to explain the odd discrepancy. They took the metabolites of ethylene glycol (the products it breaks down to after it is in the body), added them to blood samples, and ran the samples through the two different analyzers that had provided the contradictory test results that day.

"We found that it was the metabolites themselves that caused the discrepancies in the tests," he explains. The Drs. Brindley dubbed the phenomenon "the lactate gap"—when one particular analyzer shows very high lactate levels, but levels are normal on all other types. This difference can now be attributed to ethylene-glycol poisoning, which otherwise takes several hours to diagnose. "We've basically developed an immediate bedside test for ethylene glycol poisoning," says Dr. Peter Brindley, an important development since time is of the essence in treating this type of poisoning. The longer the patients go without treatment, the higher the likelihood that they will develop kidney failure or other long-term effects, or even die.

The work has proven particularly rewarding for both Drs. Brindley. Within weeks of the initial case, another patient presented at the same emergency department with similar symptoms. Aware of the recent precedent, staff immediately ran both tests and determined that ethylene glycol was the culprit. The second patient was treated and released much more quickly than the first, and recovered faster. Since he and his father published their findings, Dr. Peter Brindley has heard of about a dozen more such cases and has received e-mails from around the world, telling him of similar experiences and the successful use of the new test.

> This was a case of "translational research across the dinner table"

"Having both the science and the clinical findings seemed to amplify this work," he explains. His father adds, "I've published a couple of hundred research papers in my career. As a scientist, I always hope that my work will someday have clinical impact. This already has."

This was a case of "translational research across the dinner table", as the Brindleys put it. In the bigger picture, the excellent clinical and research environment in Alberta is building better links between clinicians and scientists all the time.

"As doctors, we provide one piece of the puzzle, and we need to be able to talk to the people who have the scientific training to provide the other piece," says Dr. Peter Brindley. "Not every city or hospital has these kinds of resources, this kind of environment. AHFMR has helped build that environment here." ❋

About the researchers

Dr. David Brindley is an *AHFMR Scientist* and a full professor in the Department of Biochemistry in the Faculty of Medicine and Dentistry at the University of Alberta. AHFMR support brought him and his family to Edmonton from England 20 years ago.

Dr. Peter Brindley is an intensive-care and critical-care physician at the University of Alberta Hospital, as well as an assistant professor in the Division of Critical Care Medicine.

Selected publication

Brindley PG, Butler MS, Cembrowski G, Brindley DN. Falsely elevated point-of-care lactate measurement after ingestion of ethylene glycol. *Canadian Medical Association Journal*. 2007 Apr 10;176(8):1097–1099.

TAKING ON infectious dis

Vaccines may be one of the most important achievements in medical science—and, given the threat of new and re-emerging infectious diseases, they are more important than ever.

"THE TIME HAS COME to close the book on infectious diseases." When US Surgeon General William H. Stewart wrote those words in his 1967 annual report, he was reflecting the mood of the time. The optimism appeared to be warranted: antibiotics had significantly reduced the incidence of many diseases in North America. It seemed only a matter of time before we got the upper hand on disease-causing micro-organisms such as viruses, bacteria, and parasites.

But that was then; this is now. Today's reality is that infectious diseases pose a rising global health threat. As it turns out, the pathogens that cause them have an extraordinary ability to change over time. We are now faced with an onslaught of newly identified infectious diseases, such as SARS, and re-emerging infectious diseases, such as tuberculosis, malaria, and cholera. Of the new diseases, 80% are *zoonotics*—diseases caused by infectious agents that can jump from animals to humans. Avian flu is an example.

"Infectious agents are much smarter than we are. Their evolutionary ability will ensure their survival." That's the opinion of Dr. Lorne Babiuk, an international authority in virology and immunology and now vice-president (research) at the University of Alberta. Before coming to Alberta, Dr. Babiuk was director of the University of Saskatchewan's Vaccine and Infectious Disease Organization (VIDO). Under his leadership, VIDO became internationally recognized for its role in the use of biotechnology to develop vaccines. The world's first genetically engineered vaccine for animals was developed at VIDO.


ease

"I believe vaccines are one of the greatest achievements of medical science"

"The kind of thinking behind the surgeon general's optimism isn't prevalent today," says Dr. Babiuk. "The scientific and medical community sees the threat. There's a renewed focus on infectious disease, which has spurred research on vaccines and resulted in a very significant increase in the number of vaccines available.

"Oddly enough, the incredible success of vaccines is a problem. Most people in North America don't come face to face with the threat of devastating infectious disease anymore. They didn't live through the days when a disease like polio terrified families, when hospitals were filled with patients in iron lungs. As a result, immunization rates are dropping. And we're hearing more and more from the anti-vaccine lobby. The reality is that there is no scientific doubt about the effectiveness of immunization. I believe vaccines are one of the greatest achievements of medical science. They dramatically cut deaths from disease. But we've become complacent, and we're putting public health at risk.

"Vaccines work. And research continues to improve them. As we understand more about the protective components of infectious agents and how the human immune system functions, we are able to be more specific in the formulation of vaccines. The amount of *antigen*—the 'active ingredient' in vaccines—needed to induce the appropriate immune response can be reduced by about 25%. We're also seeing innovations in needle-free vaccine delivery, with more vaccines designed to be administered orally or nasally.

"Basic research done in universities is critical for vaccine development. University researchers are teasing out key details about the immune system—fundamental knowledge that can be applied in the development of a wide range of vaccines. Many university researchers work on diseases that don't grab the attention of drug companies, so they play an important role in making advances in treatment for these so-called orphan diseases.

"A great deal has been accomplished, and a great deal more needs to be accomplished. We'll always be playing catch-up with infectious agents."

InterVac

Construction is underway on a $140-million centre for vaccine research and development at the University of Saskatchewan, the largest investment to date in vaccine research in Canada. The International Vaccine Centre (InterVac) will greatly enhance Canada's capacity to develop and test new vaccines. Construction is expected to be completed by 2010.

About the researcher

Dr. Lorne Babiuk is vice-president for research at the University of Alberta. He co-leads a team recently awarded an ***AHFMR Interdisciplinary Team Grant*** for vaccine design and implementation.

Selected publication

Gerdts V, van Drunen Littel-van den Hurk S, Griebel PJ, Babiuk LA. Use of animal models in the development of human vaccines. *Future Microbiology*. 2007 Dec;2(6):667-675.

Understanding the immune system

ONE OF THE REASONS for the great strides in vaccination is our increased understanding of the human immune system. "Without detailed knowledge of the immune system, it's impossible to develop a vaccine in a rational way," says Heritage Senior Scholar Dr. Babita Agrawal, a researcher at the University of Alberta. "That's why when you read papers by vaccine researchers like me, you're likely to read more about the immune system than about a vaccine. Although the amount of information about the immune system has exploded in the last 20 years, the system is very complicated, and there's a lot we still don't understand."

■ THE IMMUNE SYSTEM offers two types of immunity. *Innate immunity* is the first line of defence against infectious agents. Some immune cells respond to pathogens in a generic way—they don't recognize specific invaders. This type of response does not result in long-lasting immunity. *Adaptive immunity* is different—it remembers particular infectious agents and so can prevent reinfections. Vaccination works with this type of immunity.

Adaptive immunity relies on the ability of immune cells such as T cells and B cells to distinguish between the body's own cells and unwanted invaders. They do this by recognizing specific antigens on the surface of bacteria, virally infected host cells, or tumour cells. Specialized immune cells, called *dendritic cells*, process antigen material and present it to T cells. Once activated, the T cells then search out and destroy any cells that have the type of antigen that was presented to them.

One of Dr. Agrawal's main research interests is the hepatitis C virus. Approximately 3% of the world's population has been infected with hepatitis C. Most infections become chronic and can lead to cirrhosis, liver cancer, other liver diseases, and death. Sustained antiviral therapy can help, but it does not cure the disease.

"There's a desperate need for two kinds of hepatitis C vaccine: a *prophylactic vaccine*, one that prevents the immunized person from getting the disease, and a *therapeutic vaccine*, one that is given to already infected people, so they can fight off the infection," says Dr. Agrawal. "I'm working on both types of vaccine in my lab. We are looking at basic immune-system mechanisms, as well as how hepatitis C evades the immune system."

Hepatitis C is somehow able to get past the body's defences initially and establish itself in the body. As the infection moves into the chronic stage, the immune response weakens and becomes less effective. Dr. Agrawal believes the key to understanding how this happens will come from figuring out what might be wrong with the dendritic cells and the T cells. "Are the dendritic cells dysfunctional? Are the T cells not stimulated? Are the T cells stimulated but not functioning? What kind of immune response is required to get rid of the infection from the body? It will take a series of baby steps to answer these questions.

"The ultimate goal is to take the understanding we gain at each step and put it into a cohesive, coordinated picture. Then we can think about designing a vaccine."

About the researcher
Heritage Senior Scholar
Dr. Babita Agrawal
is an associate professor in the Department of Surgery, part of the Faculty of Medicine and Dentistry at the University of Alberta.

Selected publication

Li W, Krishnadas DK, Li J, Tyrrell DLJ, Agrawal B. Induction of primary human T cell responses against hepatitis C virus-derived antigens NS3 or core by autologous dendritic cells expressing hepatitis C virus antigens: potential for vaccine and immunotherapy. *Journal of Immunology*. 2006 May 15;176(10):6065-6075.

Defending against other pathogens

IT'S NOT ONLY VIRUSES that have developed ways to evade the immune system. Other pathogens can be just as tricky, says Dr. Tony Schryvers, who for the past 18 years has been studying bacterial infections and developing vaccines to prevent them.

■ "OUR CURRENT FOCUS is trying to overcome the bacteria's strategy of evading the host's immune response. Bacteria have decoy antigens that draw the immune response away from the preferred antigens. Even individual protein antigens have decoy regions to fool the immune system. We've developed an innovative strategy to get around this trickery."

The first step in getting through the fog is to identify the important regions of the protein antigen—the ones that must interact with host proteins in order for the bacteria to survive. "In many cases, researchers didn't know precisely what the antigens used in vaccine development did," explains Dr. Schryvers. "In our situation, we know exactly what the antigen does, and why it's so critical for survival of the bacteria."

The bacteria that Dr. Schryvers studies have developed a mechanism for obtaining iron from the host they have infected. They require iron to live, and they get it from two proteins, transferrin and lactoferrin. The specialized bacteria are responsible for a number of important diseases, including gonorrhoea and meningitis, as well as ear and lung infections.

Dr. Schryvers and his team have identified and described the pathway that transfers iron into the bacterial cell. The first step requires receptors on the surface of the bacterial cells to bind with transferrin or lactoferrin. "This gives us a clear target for a vaccine. It's the Achilles heel of these types of bacteria, and we're exploiting it. The beauty of this vaccine is that it should work for all the diseases caused by this type of bacteria."

Of course, there's still a lot of work to be done. Team members are studying the interaction between the receptors on the bacteria and the host's iron-binding proteins. The detailed structural and functional information from this work will allow them to distinguish decoy regions from regions that are required for function. The team then will use protein engineering to design an antigen that lacks the decoy regions. It should be able to stimulate the appropriate immune response.

"We've done preliminary experiments to show that the regions we want to target can produce an immune response that protects against very different strains of bacteria," says Dr. Schryvers. "I've assembled a team of experts in various fields, including protein crystallography, nuclear magnetic resonance, protein engineering, and immunology. We're coming at this from different angles, but our goal is the same: to develop an effective, broad-spectrum, long-lasting vaccine."

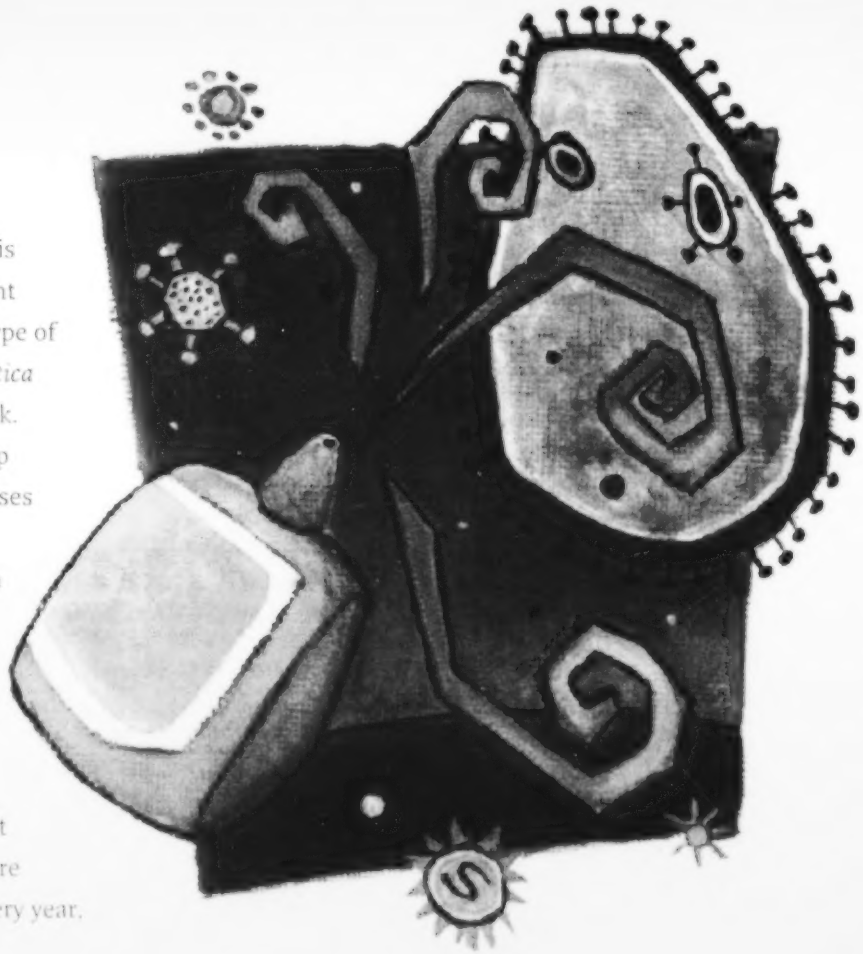
"It's the Achilles heel of these types of bacteria, and we're exploiting it"

About the researcher
Dr. Tony Schryvers is a full professor in the Department of Microbiology and Infectious Diseases in the University of Calgary Faculty of Medicine. He is the team leader of the group recently awarded an ***AHFMR Interdisciplinary Team Grant*** for vaccine design and implementation.

Selected publication

Khan AG, Shouldice SR, Kirby SD, Yu R, Tari LW, Schryvers AB. High-affinity binding by the periplasmic iron-binding protein from *Haemophilus influenzae* is required for acquiring iron from transferrin. *Biochemical Journal*. 2007 Jun 1;404(Pt 2):217–225.

Amoebas and dysentery



JUST DOWN THE HALL FROM DR. SCHRYVERS, Dr. Kris Chadee is working on a vaccine for a different kind of pathogen: an amoeba (a type of parasite) called *Entamoeba histolytica* that can contaminate food or drink. Once it enters the body, it takes up residence in the intestine and causes a severe form of diarrhea called *amoebic dysentery*. If the condition is left untreated, the amoebas can burrow through the intestinal wall, spread through the bloodstream, and form abscesses in organs such as the liver, lungs, and brain. At least 100,000 people die and millions are made ill by amoebic dysentery every year, mainly in developing countries.

■ DR. CHADEE has been studying this amoeba for the past 20 years. His first breakthrough came very early on, when he identified the protein on the surface of the parasite that allows it to attach to the intestine. It's called a *galactose-binding lectin:* lectin is a type of sugar-binding protein, and galactose is the name of the sugar it binds to. Galactose is found on the receptors in both the mucous layer and the epithelial cells that line the intestines.

"Pathogens that infect the gut must be able to anchor themselves; otherwise they'll be swept away," explains Dr. Chadee. "This amoeba is very tenacious. Because the lectin can bind to both the mucous and epithelial cells, the amoeba can deliver a double whammy to an infected person."

Dr. Chadee knew that if he could find a way to stop the lectin from binding, he would have the basis of a vaccine. His team worked for years to determine which parts of the lectin are necessary for sugar binding. They then packaged the antigen in an intranasal vaccine (delivered by squirting it up the nose) and tested it on gerbils—with some exciting results.

"The vaccine was 100% effective," says Dr. Chadee. "We found antibodies not only at the mucosal surface in the intestines but also in the blood and liver. This is really important because it shows that the vaccine can target both phases of the disease—when it's in the gut and when it spreads to other organs. We were ecstatic."

"All these 'developing world' diseases are importable or acquirable"

The next steps will be a pre-clinical trial followed by clinical trials in humans. A basic researcher like Dr. Chadee would normally enter into an agreement with a drug company to complete these stages, which can cost hundreds of millions of dollars. But here's where money, politics, and logistics all clash with science. A vaccine for a disease like amoebic dysentery that affects mainly people in the developing world is not going to be a big money-maker. Dr. Chadee has had a difficult time attracting serious interest from drug companies.

"We've hit a brick wall, and it's very disheartening. I knew this could happen—I just didn't think it would affect me personally."

Dr. Chadee may be down but he is not out. He has had preliminary talks with the Bill and Melinda Gates Foundation. The Foundation's Global Health Program supports research on vaccines to fight diseases in developing countries.

"As North Americans, we tend to think that diseases like dysentery are not our problem. Yet we are a nation of immigrants, and we are also global tourists. All these 'developing world' diseases are importable or acquirable. And with climate change, they could be in our backyard. Any potential cure or intervention needs to be looked at seriously."

About the researcher

Dr. Kris Chadee is a full professor in the Department of Microbiology and Infectious Diseases in the Faculty of Medicine at the University of Calgary. He chairs the university's Gastrointestinal Research Group and holds a Canada Research Chair in Gastrointestinal Inflammation.

Selected publication

Ivory CPA, Chadee K. Intranasal immunization with Gal-inhibitable lectin plus an adjuvant of CpG oligodeoxynucleotides protects against *Entamoeba histolytica* challenge. *Infection and Immunity.* 2007 Oct;75(10):4917–4922.

> More than prevention

Although vaccines usually make us think of preventing illness, many vaccines reduce the severity of disease rather than preventing it. Examples include vaccines for malaria and shingles. "That doesn't mean these vaccines are ineffective," says Dr. Jennie Johnstone, a clinical research fellow in infectious diseases at the University of Alberta. "Immunized people who contract the disease are likely to be less sick and [will tend to] avoid long-term health consequences."

● **A case in point** is the vaccine for *Streptococcus pneumoniae*, the most common cause of community-acquired pneumonia (the name given to pneumonia acquired outside of a hospital setting). This type of pneumonia occurs throughout the world and is a leading cause of illness and death. The adult pneumococcal vaccine has been available since the mid-1980s. Research evidence shows that, although the vaccine does not prevent pneumonia, it does reduce the rate of invasive pneumococcal diseases (such as pneumococcal meningitis, an infection of the membranes covering the brain and spinal cord) and pneumococcal bacteremia (a blood infection). Dr. Johnstone set out to investigate a new hypothesis: that prior vaccina-

Many vaccines reduce the severity of disease rather than preventing it

tion might improve outcomes in patients who develop pneumonia.

She worked with a very large database—approximately 3,400 adults with community-acquired pneumonia who were admitted to the six Capital Health hospitals in the Edmonton region between 2000 and 2002. Statistical methods were used to determine the association between prior vaccine use and outcome. Vaccinated patients with community-acquired pneumonia had a death rate and a rate of admission to the intensive-care unit that were both about 40% lower than those of patients who had not been vaccinated.

"It's very clear: the people who were vaccinated had much better outcomes," says Dr. Johnstone. "The results indicate we could be doing better for many more patients, since only 22% of our population were vaccinated before their hospitalization. Moreover, fewer than 10% of eligible patients were vaccinated before they were discharged from hospital." Current guidelines recommend the vaccine for anyone at increased risk for pneumonia, including those 65 and older, people with cardiovascular and lung diseases, and those whose immune systems are not functioning correctly.

"Now I can say with confidence to my infectious-disease colleagues that this is a very worthwhile vaccine. The perception that it is ineffective is wrong. The vaccine needs to be promoted—to get vaccination rates up to where they should be."

The pneumonia study was Dr. Johnstone's first foray into *epidemiology*, the study of factors affecting the health and illness of populations. In the fall, she hopes to begin working toward a master's degree in epidemiology at McMaster University in Ontario. "The degree will give me the tools I need to start a serious program of epidemiological research. Eventually I'd like to combine clinical work and research, hopefully back in Alberta."

About the researcher

Dr. Jennie Johnstone is a clinical research fellow in infectious diseases at the University of Alberta. Her research was supervised by ***Heritage Health Scholar*** Dr. Sumit Majumdar, from the Department of Medicine in the University of Alberta's Faculty of Medicine and Dentistry, and Dr. Tom Marrie, dean of the Faculty. Support for the study came partly from an *AHFMR Independent Establishment Grant*.

Selected publication

Johnstone J, Marrie TJ, Eurich DT, Majumdar SR. Effect of pneumococcal vaccination in hospitalized adults with community-acquired pneumonia. *Archives of Internal Medicine*. 2007 Oct 8;167(18):1938–1943

> A Canadian success story

"Our work ushered in the era of antiviral therapy for hepatitis B"

Although an effective vaccine against the hepatitis B virus exists, the disease remains a major health problem throughout the world. Nearly 400 million people are infected, and more than 3,000 people die of it daily. The hepatitis B virus is the leading cause of chronic liver disease, which can cause cirrhosis that may lead to liver cancer. Antiviral drugs are used to prevent progress to these illnesses. Unlike vaccines, which mobilize a person's immune system to fight a virus, antivirals target viral proteins directly to inhibit virus growth.

● **The first oral antiviral agent** for hepatitis B, lamivudine, is a true Canadian success story with roots in Alberta. The research was begun in 1986 by Dr. Lorne Tyrrell and Dr. Morris Robins at the University of Alberta. Their work resulted in the discovery of several potent antivirals against hepatitis B and led to a major collaboration with Glaxo Canada (now GlaxoSmithKline). One of the antivirals was lamivudine, a drug that had been developed for treating AIDS patients.

In 1989 Dr. Tyrrell's team showed that lamivudine is a very effective antiviral for the hepatitis B virus. Successful animal testing and human trials followed. Lamivudine is now the primary drug used to treat chronic hepatitis B carriers. It is licensed in 170 countries worldwide. "We have a lot to be proud of with this story," says Dr. Tyrrell. "Our work ushered in the era of antiviral therapy for hepatitis B."

But there is a problem with lamivudine: A very small genetic change in the hepatitis B virus renders it resistant to the drug. Newer drugs that are less prone to resistance have been developed; however, lamivudine remains widely prescribed because it is reasonably priced and very well tolerated.

"Resistance was a real disappointment, because we were hoping we had a treatment and would cure all patients of hepatitis B," says Dr. Tyrrell. "We're still working on this."

One of Dr. Tyrrell's graduate students is taking a unique approach to eliminating the hepatitis B (HBV) infection. Kim Zimmerman, who is supported by an AHFMR Studentship, is studying one of the forms that HBV takes in liver cells. While antivirals tend to be effective at getting rid of HBV in the fluid that fills the liver cells, they don't work for HBV in the nucleus of the cells. (*See* story on page 24.)

Dr. Tyrrell also collaborated with University of Alberta colleagues Dr. Norm Kneteman and Heritage Clinical Fellow Dr. David Mercer to develop the first non-primate animal model for hepatitis C research. The three scientists have formed a company, KMT Hepatech Inc., to do contract research work using this model. They were recently awarded a contract from the US National Institutes of Health to help independent researchers test antivirals. ❋

About the researcher
Dr. Lorne Tyrrell is a full professor in the Department of Medical Microbiology and Immunology, part of the Faculty of Medicine at the University of Alberta.

Cancer, aging, and immortality

Dealing with immortal cells is all in a day's work for Dr. Karl Riabowol. Unfortunately, immortal cells usually point to cancer.

OUR BODIES are made up of more than 200 different kinds of cell, each type with its own set of replication instructions. Some cells, such as nerve and muscle cells, don't replicate at all once the organism has reached biological maturity. For others replication is an ongoing process; skin cells, for example, shed and replace themselves constantly. Then there are "immortal" cells, the kind that multiply with no sign of stopping.

AS ENTICING AS IT MIGHT SOUND, however, this unrestrained growth of immortal cells is typically associated with cancer—making it a kind of immortality we're better off avoiding. AHFMR Scientist Dr. Karl Riabowol studies immortal cells in hopes of understanding how to suppress the growth of life-threatening tumours.

Dr. Riabowol spent several years studying and conducting research at the Cold Spring Harbor Laboratory in New York. Home to seven Nobel Prize winners, this private, non-profit research institution is renowned as one of the world's meccas for molecular biology. Dr. James D. Watson, one of the co-discoverers of the double-helix structure of DNA, spent nearly 40 years at this institution as its outspoken director, president, and chancellor.

ING genes can kill cancerous tumours

"Immortal" cells multiply with no sign of stopping

Attracted by mountains, foothills, and a handsome AHFMR grant that would cover the cost of setting up and operating a new lab, Dr. Riabowol left New York for Alberta in 1991. Today he directs the Aging and Immortalization Laboratory in the University of Calgary's Faculty of Medicine.

When he first arrived in Calgary, Dr. Riabowol wanted to isolate genes that could act as growth inhibitors—what cancer scientists call "tumour suppressors". Using a new isolation procedure they had developed, Dr. Riabowol and his group had a breakthrough in 1996 with their discovery of a new tumour-suppressing gene: ING-1. The finding represented quite a feat in molecular biology, occurring as it did well before the human genome was published in 2001. ING-1 was not named after the financial institution; rather, the gene's name is derived from "INhibitor of Growth". As ING-1 began to demonstrate its ability to kill tumours, it stimulated a search for related genes. Dr. Riabowol subsequently discovered and named four more INGs: ING-2 to ING-5.

ING tumour suppressors are often "turned off" in certain cancers. This led Dr. Riabowol to ask questions from a different perspective: Do the cancers somehow know to target the cells that had their tumour suppressors turned off? And if these "brakes" to growth are not activated, does cancer formation necessarily follow? He also wants to know if normal aging cells use tumour suppressors to limit their growth.

ING tumour suppressors are often "turned off" in certain cancers

In his search for answers, Dr. Riabowol hopes that the INGs discovered some 10 years ago will help him find clues to how aging relates to cancer formation. His lab also studies cell-lifespan regulators known as *telomeres*, tiny structures at each end of our chromosomes that appear to diminish in size each time a cell replicates. Like clocks ticking off seconds and minutes, telomeres count off the limited number of cell-replication events dictated by our genes.

Although he has not yet proven a definitive link between cell replication and human lifespan, Dr. Riabowol and his team have discovered that children conceived by older fathers have longer telomeres. This breakthrough is likely to have profound implications for society, since longer telomeres appear to be linked to longer—and probably healthier—lifespans, and might also protect against the emergence of cancer.

The idea of cancer as primarily a disease of aging hits home with just one telling statistic: Overall cancer incidence for people in their eighties is about 800 times higher than for people in their twenties. Dr. Riabowol was an early proponent of the view that cancer and cell aging are closely linked, and the concept is rapidly gaining credence in the scientific community today.

What are the potential implications as scientists around the world research this concept? Establishing how a person's age is linked to tumour suppression and cell immortality is the next step on the road to designing small multi-functional molecules for treating age-specific cancer in the future. ✲

About the researcher
Dr. Karl Riabowol is an *AHFMR Scientist* and a professor in the Department of Biochemistry and Molecular Biology, as well as the Department of Oncology, in the University of Calgary's Faculty of Medicine.

Selected publication

Soliman MA, Riabowol K. After a decade of study-ING, a PHD for a versatile family of proteins. *Trends in Biochemical Sciences*. 2007 Nov;32(11):509–519.

Recommended websites

Aging Research Centre
http://www.arclab.org

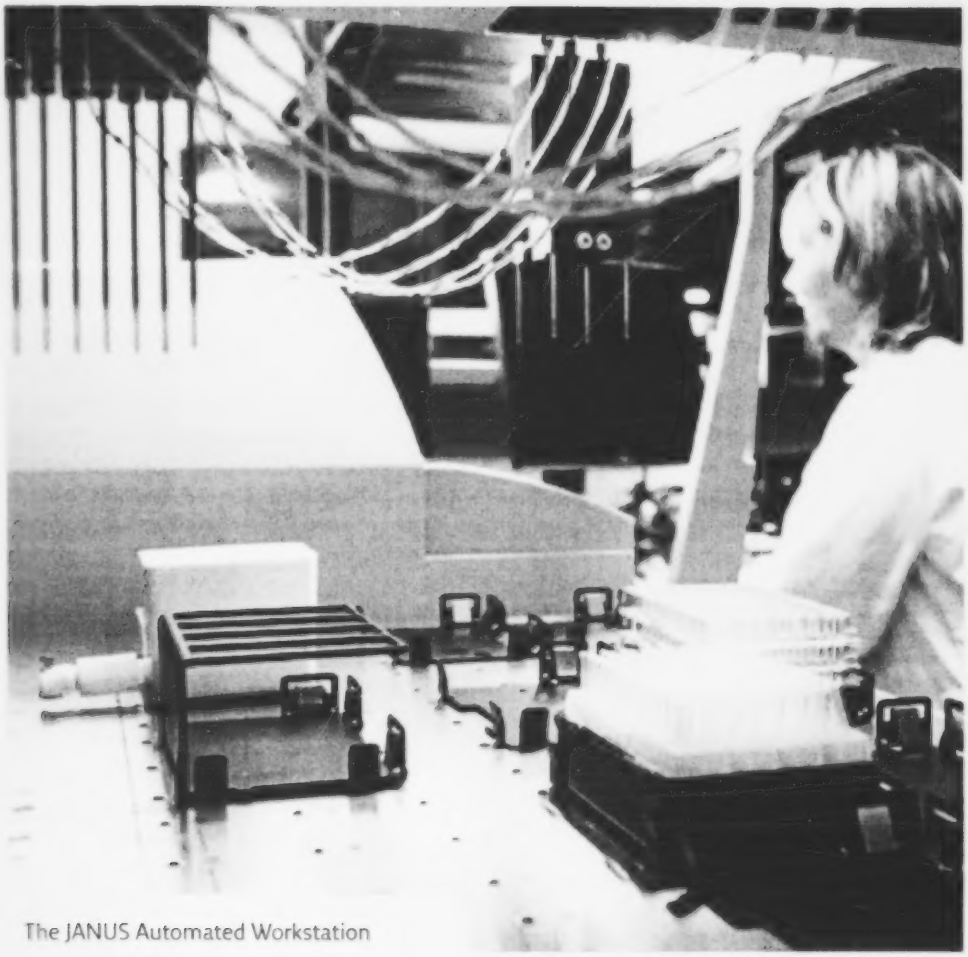
Alliance for Aging Research
http://www.agingresearch.org

Cool tools

96 ways to avoid tedium and strain

Named after the Roman god of beginnings and endings, the JANUS Automated Workstation has been an eagerly awaited arrival in the Antibody Services lab at the Southern Alberta Cancer Research Institute.

Properly called a "robotic workstation," this product shoots fluids out of its multiple fingers into a corresponding number of wells. The transport of accurate amounts of fluids using a pipette (a narrow glass tube) is a necessity in most research labs. The 96-well configuration of the JANUS will be like adding 96 pipetting staff to the lab team, none of whom will be at risk for repetitive-strain injuries. Even better, this particular setup can be expanded to 384 wells.



The JANUS Automated Workstation

"This robot makes us smile," says Dr. Karl Riabowol, lab director. "Not only will it improve pipetting accuracy and increase production, but we expect it will help improve staff morale by freeing them from tedious, repetitive tasks."

The increased capacity this robotic arm provides means that the Antibody Services lab can serve more researchers and increase its revenues as well. A key resource for the University of Calgary's Faculty of Medicine, the lab also counts among its clients AHFMR researchers, Government of Canada scientists, and biopharmaceutical companies.

The lab's new robotic helper has already received its first assignments. One of its main duties will be to screen for monoclonal antibodies (substances that can find and attach to cancer cells), a time-consuming task required by many biochemistry researchers. But, in the same way as our expectations and uses for e-mail have grown over the years, Dr. Riabowol believes the future will provide many more tasks for the group's robotic partner. ✻

AHFMR Scientist **Dr. Karl Riabowol** received an *AHFMR Major Equipment Grant* to purchase the JANUS Automated Workstation.

Clamping down on hepatitis B

An AHFMR Student looks for ways to disable a stubborn form of the dangerous liver virus.

Kim Zimmerman

Hepatitis B virus is the world's most prevalent serious liver infection. About 2 billion people around the world have been infected, generally through the transmission of blood or other body fluids. With the help of current treatments, most of those 2 billion will manage to clear the virus and recover. But around 10% will not; they will develop chronic infections that can lead to even more serious long-term illnesses, such as liver cancer. For infants and children, the percentage is much higher: 90% of infants and 50% of young children infected with hepatitis B will develop chronic infections.

These chronic infections are caused by a special form of the hepatitis B virus that develops in the liver: a virus consisting of a very stable type of DNA (called *cccDNA*) that is extremely difficult to attack directly with drugs or treatments. But AHFMR Student Kimberley Zimmerman may have found a way to do just that.

Zimmerman studies zinc finger proteins—so called because each protein is composed of a number of finger-like structures, with zinc ions in the middle to hold them together. Each zinc finger can recognize and attach to a specific type of DNA; the more zinc fingers, the more DNA that can be recognized. Zimmerman designs these proteins to attach to specific DNA combinations—namely, the cccDNA that is the culprit behind chronic hepatitis B infections.

"Because we know the DNA sequence of hep B virus, we can decide what sequence of zinc finger protein is needed

Zimmerman designs proteins to attach to specific DNA like this clamp on an apple

to bind it," says Zimmerman. She explains that the concept is similar in principle to the Denver boot, a type of wheel clamp used by some police departments to immobilize illegally parked vehicles. When a Denver boot is placed on a wheel, the car can't go anywhere. "The idea is that these zinc finger proteins are the clamp, and that particular form of hep B virus in the liver is the tire."

Once she was convinced that the proteins were attaching well to their targets, Zimmerman tried the process in a model of a hepatitis B infection to see how it affected production of the virus. And sure enough, she found that the proteins travelled to the hepatitis B DNA and bonded to it strongly, preventing the DNA from reproducing the hepatitis B virus. The next step is to determine whether the zinc finger proteins can make the DNA break down and disappear.

In September, Zimmerman filed a patent for the application of zinc finger proteins as future treatments. "The proteins are the first therapeutic to target cccDNA," she says. "We've seen very good results so far with inhibition of the virus, and it's exciting to take the next step." ❋

About the researcher
Kimberley Zimmerman is an *AHFMR Student* in the Department of Medical Microbiology and Immunology in the University of Alberta Faculty of Medicine and Dentistry. She is working toward her Ph.D. under the supervision of Dr. Lorne Tyrell.

Selected publication
Zimmerman KA, Fischer KF, Joyce MA, Tyrrell DJL. Hepatitis B virus-binding polypeptides and methods of use thereof. *U.S. Patent Application.* 2007;60/972,644.

Recommended web sites
Hepatitis B Foundation
http://www.hepb.org

World Health Organization - Hepatitis B
http://www.who.int/immunization/topics/hepatitis_b/en/index.html

AHFMR funding partners

The Alberta Heritage Foundation for Medical Research (AHFMR) has contributed more than $900 million to Alberta's health-research community. The Foundation also relies on the contributions of many partners in building and sustaining health research in this province. To mention just a few, these partners include

- the Government of Alberta and its related ministries and programs;
- federal granting agencies such as the Canadian Institutes of Health Research, the Canada Foundation for Innovation, and the Canadian Health Services Research Foundation;
- international funding partners like the Wellcome Trust and the National Institutes of Health; and
- non-profit and voluntary funding agencies such as NeuroScience Canada, the Heart and Stroke Foundation, the Canadian Diabetes Association, and the National Cancer Institute of Canada.

Following **up**

Complementary therapies, quality of life, and cancer care

■ Decisions affecting quality of life can be some of the hardest to make, especially for patients diagnosed with cancer. Conventional cancer treatments include radiation, chemotherapy, and surgery, augmented with new and ever-improving medical technologies. Thanks to modern medicine, increasing numbers of people now survive with the disease for many years.

But the face of cancer care is changing, and part of the change can be attributed to a steep rise in the use of complementary and alternative medicine (often called CAM). A wide range of CAM therapies is available—from aromatherapy and acupuncture to chiropractic, massage therapy, and reflexology; from an astonishing variety of special diets to nutritional supplements prescribed by naturopathic doctors and practitioners of traditional Chinese medicine.

So, what motivates cancer patients to choose therapies outside of conventional Western medicine? Until recently, the answer was anecdotal and sketchy at best. In 2003, with support from AHFMR, Dr. Marja Verhoef

Dr. Marja Verhoef

began to investigate what type of information cancer patients consider important when deciding upon their care.

It turns out that cancer patients are not necessarily inspired by scientific evidence. Those who have used complementary and alternative therapies previously are likely to be less concerned with scientific evidence than with personal experience and testimonials from other people, and and are more willing to trust their gut feelings and the results of trial and error. Newly diagnosed patients with little experience of alternative treatments tend to be more interested in scientific evidence and their doctors' advice.

Dr. Verhoef's work shows that, more and more, cancer patients seek treatments that fit with their beliefs about healing, causes of cancer, and mind-body-spirit approaches. ❋

About the researcher

Dr. Marja Verhoef is a professor in the Department of Community Health Sciences at the University of Calgary. She received support for this study from the ***Health Research Fund***, administered by AHFMR on behalf of Alberta Health and Wellness.

Selected publication

Verhoef MJ, Mulkins A, Carlson LE, Hilsden RJ, Kania A. Assessing the role of evidence in patients' evaluation of complementary therapies: a qualitative study. *Integrative Cancer Therapies*. 2007 Dec;6(4):345-353.

Recommended websites

The CAM in UME Project: Complementary and Alternative Medicine Issues in Undergraduate Medical Education
http://www.caminume.ca/

Canadian Interdisciplinary Network for Complementary & Alternative Medicine Research
http://www.incamresearch.ca/

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